

Preliminary Amendment

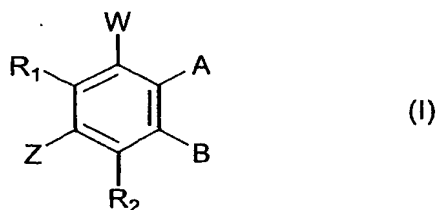
National Stage Entry of PCT/AU2003/001296

Attorney Docket No.: Q86664

AMENDMENTS TO THE CLAIMS

Claims

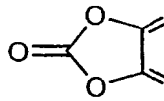
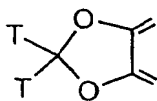
1. (original): A method of increasing the sensitivity of cancer cells or a tumour to a chemotherapeutic agent by contacting said cells or tumour with an isoflavonoid compound of formula (I):



in which

R₁, R₂ and Z are independently hydrogen, hydroxy, OR₉, OC(O)R₁₀, OS(O)R₁₀, CHO, C(O)R₁₀, COOH, CO₂R₁₀, CONR₃R₄, alkyl, haloalkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, alkylaryl, alkoxyaryl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or

R₂ is as previously defined, and R₁ and Z taken together with the carbon atoms to which they are attached form a five-membered ring selected from



, or

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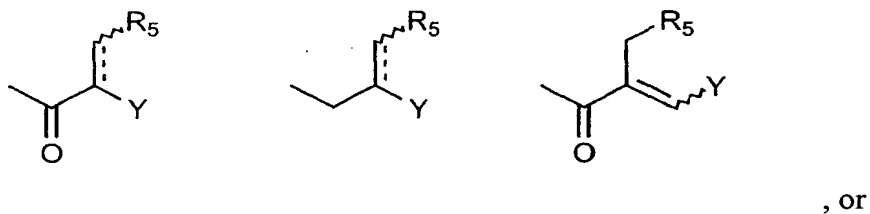
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R_1 is as previously defined, and R_2 and Z taken together with the carbon atoms to which they are attached form a five-membered ring selected from

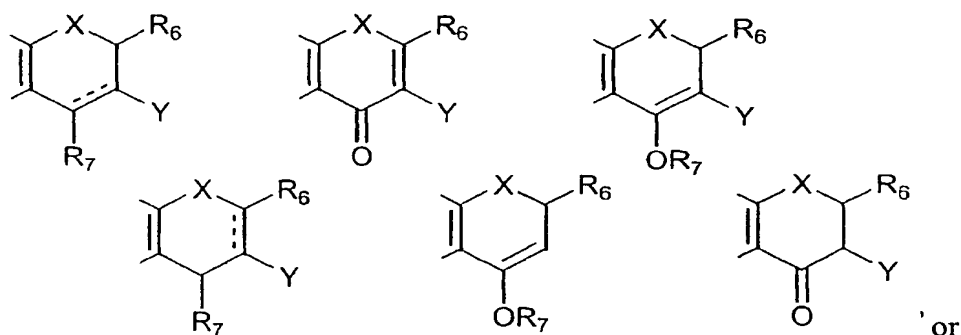


and

W is R_1 , A is hydrogen, hydroxy, NR_3R_4 or thio, and B is selected from



W is R_1 , and A and B taken together with the carbon atoms to which they are attached form a six-membered ring selected from

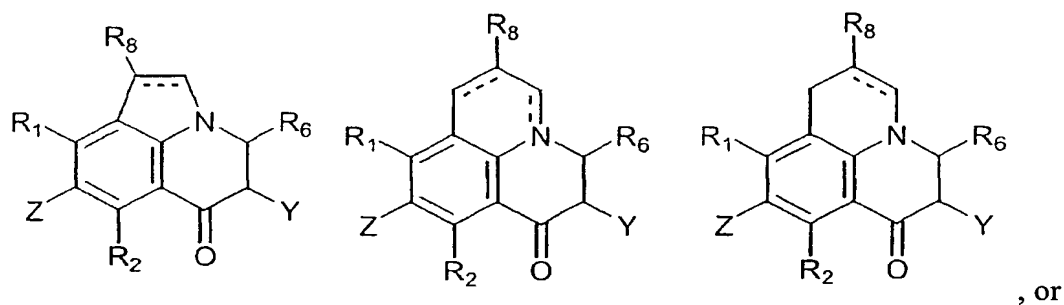


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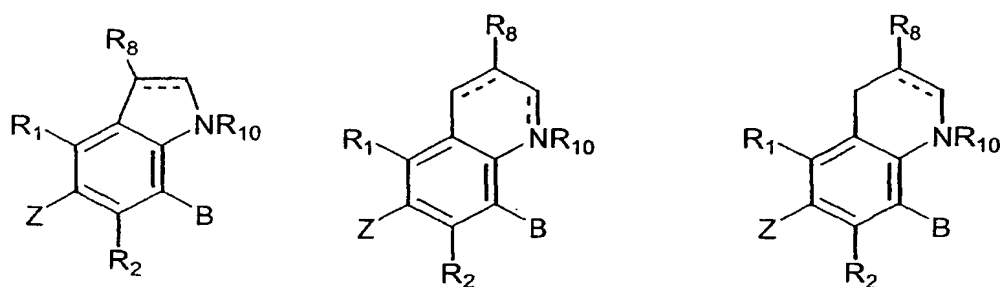
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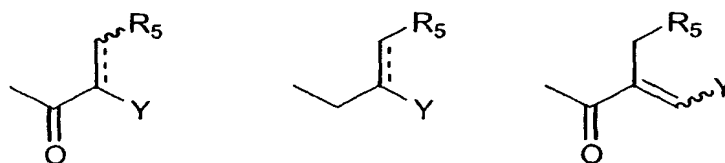
W, A and B taken together with the groups to which they are associated are selected from



W and A taken together with the groups to which they are associated are selected from



and B is selected from



wherein

R₃ is hydrogen, alkyl, arylalkyl, alkenyl, aryl, an amino acid, C(O)R₁₁ where R₁₁ is hydrogen, alkyl, aryl, arylalkyl or an amino acid, or CO₂R₁₂ where R₁₂ is hydrogen, alkyl, haloalkyl, aryl or arylalkyl,

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R₄ is hydrogen, alkyl or aryl, or

R₃ and R₄ taken together with the nitrogen to which they are attached comprise pyrrolidinyl or piperidinyl,

R₅ is hydrogen, C(O)R₁₁ where R₁₁ is as previously defined, or CO₂R₁₂ where R₁₂ is as previously defined,

R₆ is hydrogen, hydroxy, alkyl, aryl, amino, thio, NR₃R₄, COR₁₁ where R₁₁ is as previously defined, CO₂R₁₂ where R₁₂ is as previously defined or CONR₃R₄,

R₇ is hydrogen, C(O)R₁₁ where R₁₁ is as previously defined, alkyl, haloalkyl, alkenyl, aryl, arylalkyl or Si(R₁₃)₃ where each R₁₃ is independently hydrogen, alkyl or aryl,

R₈ is hydrogen, hydroxy, alkoxy or alkyl,

R₉ is alkyl, haloalkyl, aryl, arylalkyl, C(O)R₁₁ where R₁₁ is as previously defined, or Si(R₁₃)₃ where R₁₃ is as previously defined,

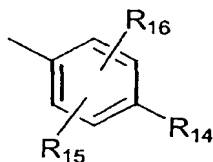
R₁₀ is hydrogen, alkyl, haloalkyl, amino, aryl, arylalkyl, an amino acid, alkylamino or dialkylamino,

the drawing “---” represents either a single bond or a double bond,

T is independently hydrogen, alkyl or aryl,

X is O, NR₄ or S, and

Y is



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wherein

R₁₄, R₁₅ and R₁₆ are independently hydrogen, hydroxy, OR₉, OC(O)R₁₀, OS(O)R₁₀, CHO, C(O)R₁₀, COOH, CO₂R₁₀, CONR₃R₄, alkyl, haloalkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or any two of R₁₄, R₁₅ and R₁₆ are fused together to form a cyclic alkyl, aromatic or heteroaromatic structure, and pharmaceutically acceptable salts thereof.

2. (original): A method of claim 1, wherein the sensitivity of the cancer cells or tumour to the chemotherapeutic agent is restored.

3. (currently amended): A method of claim 1, wherein the compound of formula (I) is administered to a subject in need of such treatment.

4. (original): A combination therapy for the treatment, prophylaxis, amelioration, defence against and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress comprising administering to a subject a therapeutically effective amount of a compound of formula (1) as defined in claim 1 and a chemotherapeutic agent.

5. (original): A method for the treatment, prophylaxis, amelioration, defence against and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress which method includes the step of administering a compound of formula (I) and a chemotherapeutic agent.

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6. (original): A method of claim 5, wherein the cancer is selected from breast cancer, prostatic cancer, testicular cancer, ovarian cancer, uterine cancer and colorectal cancer.

7. (original): A method claim 6, wherein the cancer is selected from ovarian cancer, prostatic cancer and pancreatic cancer.

8. (original): A method of claim 5, wherein the administration of the compound of formula (1) precedes the administration of the chemotherapeutic agent.

9. (original): A method of claim 5, wherein the administration of the compound of formula (I) and the chemotherapeutic agent is simultaneous.

10. (original): A method claim 5, wherein the combination therapy follows observed resistance by cancer cells or tumour to a chemotherapeutic agent.

11. (original): A method of claim 5, wherein the compound of formula (I) is an isoflav-3-ene of general formula (VIa).

12. (original): A method of claim 11, wherein the compound is dehydroequol.

13. (original): A method of claim 5, wherein the chemotherapeutic agent is cisplatin, paclitaxel or carboplatin.

14. (canceled).

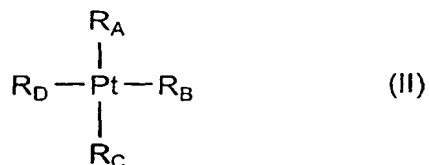
15. (original): A pharmaceutical agent comprising a compound of formula (I) and an anticancer agent.

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16. (original): A platinum-isoflavonoid complex or analogue thereof of the general formula (II):



in which

R_A , R_B , R_C , and R_D are independently halo, hydroxy, XR_E , alkoxy, $OC(O)R_F$, $OS(O)R_F$, thio, alkylthio, amino, alkylamino or dialkylamino,

X is O, NR_F or S, and

R_F is hydrogen, alkyl, arylalkyl, alkenyl, aryl or an amino acid,

wherein

at least one of R_A , R_B , R_C , and R_D , and preferably only R_A , is XR_E where R_E is an isoflavonoid compound represented by general formula (I) set out above or is derived from or is a radical or ion of the isoflavonoid compound (I) and ligates to the platinum through any one or more of the heteroatoms X or a radical of the heteroatoms defined as part of R_E or alternatively by a double bond on the isoflavonoid compound (I)

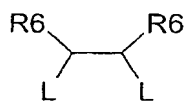
and

when R_A is XR_E , R_B , R_C and/or R_D together may form part of a bidentate or tridentate ligand of general formulae (B) and (T) respectively

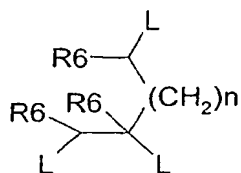
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(B)



(T)

wherein L represents a ligating atom chosen from N, O and S,

n is from 0 to 8, and

each R₆ is independently as defined above or may together form part of a cyclic alkyl, aromatic or heteroaromatic structure,

which platinum-isoflavonoid complexes include pharmaceutically acceptable salts thereof.

17. (original): A method for the treatment, prophylaxis, amelioration, defence against, and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress which method comprises administering to a subject a therapeutically effective amount of one or more platinum-isoflavonoid complexes of the formula (II) as defined above.

18. (canceled).

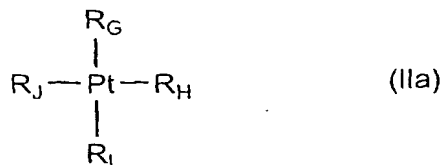
19. (original): A pharmaceutical composition comprising one or more platinum-isoflavonoid complexes of the formula (II) in association with one or more pharmaceutical carriers and/or excipients.

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20. (original): A composition comprising a platinum complex of the general formula (IIa),



in which

R_G , R_H , R_I , and R_J are independently halo, hydroxy, alkoxy, $OC(O)R_K$, $OS(O)R_K$, thio, alkylthio, amino, alkylamino or dialkylamino,

X is O, NR_K or S, and

R_K is hydrogen, alkyl, arylalkyl, alkenyl, aryl or an amino acid,

in association with an isoflavonoid compound of general formula (I) as defined in claim 1 and pharmaceutically acceptable salts thereof.

21. (original): A method for the treatment, prophylaxis, amelioration, defence against, and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress which comprises administering to a subject a therapeutically effective amount of a composition of claim 20.

22. (canceled).